HIV's Evolving Evolution

A new computer model examines HIVâ€™s rate of mutation over time.

The human immunodeficiency virus (HIV)—the virus that causes AIDS—is such a tenacious pathogen because its genetic material readily mutates when the virus reproduces. Once inside the body, the HIV population quickly evolves and diversifies into thousands of different viruses, so-called quasi-species, making it nearly certain that some viruses will evade the body's immune system and resist antiviral drugs.

Curiously, during the later stages of HIV infection, the quasi-species begin to accumulate fewer new genetic differences from the original viral strain (the divergence of genetic sequences begins to saturate), and the number of different viruses (the viral diversity) begins to decline. These changes always precede the progression of the disease to AIDS, although the time for AIDS to develop varies greatly from patient to patient.

Understanding the dynamics of these changes could help scientists develop new ways to stop the virus. That was why Los Alamos researchers Ha Youn Lee, Alan S. Perelson, and Thomas Leitner, all of the Theoretical Biology and Biophysics group, and collaborator Su-Chan Park from Cologne University, Germany, developed a simple model of HIV sequence evolution. The model had two main components: (1) fitness, the number of offspring produced, and (2) the proportion of offspring that are mutants. They tested the model using data from the Los Alamos HIV Sequence Database, which holds more than 250,000 genetic sequences of HIV from patients around the globe.

The results were surprising. In short, fitting the model to data showed that after evolving at a constant rate, the quasi-species' rate of evolution slowed down.

HIV infects cells of the immune system, reproduces within them, and then kills the cells, a course of action that suggests several possible reasons for the slowdown. One possibility is that because there are fewer immune cells in the later stages of the infection, the reproduction rate decreases. Another is that the weakened immune system is no longer able to apply "selective pressure" to drive the evolution. In any case, the work has already reconciled previously conflicting observations of the relationships between the rate of HIV evolution and disease progression.

The work is reported in a recent paper, "Dynamic Correlation between Intrahost HIV-1 Quasispecies Evolution and Disease Progression," PLoS Computational Biology 4 (12), e1000240 (2008).